DISCUSSION OF PAPER BY J. K. FRENKEL, M.D., Ph.D.: BREAKING THE TRANSMISSION CHAIN OF *TOXOPLASMA*: A PROGRAM FOR THE PREVENTION OF HUMAN TOXOPLASMOSIS*

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INFECTIOUS diseases can be prevented or modified by any or all of several methods. If the illness is one in which protective antibodies are produced during its natural course, we can attempt to simulate this with a vaccine. Either live or killed organisms can be used, but the former usually are superior to the latter. The outlook for this in relation to *Toxoplasma* is not very promising, especially since clinical residua are quite uncommon in most areas and exceedingly rare in others; this causes much apathy toward immunization. Perhaps more important, nature provides all the attributes of a potent live vaccine in that it is uncommon for postnatally-acquired human infections, at least, to be symptomatic. This may be because the sources of infection are in other species, requiring adaptation to man to produce illness. Whatever the reason, the natural disease, in essence, is vaccine-like and immunizing. The one problem is that this may occur during pregnancy, but certainly there would appear to be little likelihood of improving on the spontaneous event except to be able to accomplish it at will. One simplifying positive aspect of this part of the problem is that all available evidence points to a single antigenic type. Hence I am at a loss to interpret the reason for Dr. Frenkel's statement: "Preliminary work in progress includes a seriologic and immunologic comparison of a large number of *Toxoplasma* isolates to determine whether one or several types exist."

Another approach to the control of an infectious disease may be

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through the elimination of the pathogen from the environment. A good example of this would be the demonstrated effectiveness of the treatment of *Histoplasma*-infected soils with formaldehyde. At this time there appears to be no reason to include environmental sterilization in the control of *Toxoplasma*, except as specifically noted below.

Apparently the two situations with which we are confronted are those related to the feces of infected cats and to meat. In the case of the latter, while much is made of the risk of *handling* uncooked meat, I know of no valid evidence that those who have the greatest amount of such exposure are at any increased risk of infection. This might be an interesting investigation in itself. Certainly, more needs to be known about the sterilizing effects of freezing meat. Until then it would appear reasonable for a pregnant woman to avoid uncooked or rare meat if she is unaware of her antibody status.

It is in respect to the other problem: namely, cat feces, that instructions and conclusions tend to become a little difficult. What we know about this aspect is that during acute infections cats excrete a resistant oocyst which can infect other animals. As for primates, infectivity of oocysts was demonstrated in one chimpanzee in the laboratory, and several humans *may* have acquired infections while working with such forms. This, as far as I am aware, summarizes the actual experience. Some have extrapolated freely from this as in the following recent example from the scientific literature: "Inoculation with the oocysts found in the feces of the domestic cat is now considered the major route in transmission of the disease."[1] Also, Dr. D. R. Peterson[2] recently wrote: "Reportedly, Eskimos do not keep domestic cats as house pets. Accordingly, if Felidae play a primary role in transmission of infection to humans, toxoplasmosis antibody prevalence among Eskimos should be virtually absent." If others do not go quite so far, they probably do not disagree with either statement.

Some have used a family described by Fleck, Chessum, and Perkins last year[3] to further the cat-human concept. It might be useful to dwell on this for a moment. I wrote to Dr. Fleck to obtain his responses to some questions which troubled me. He kindly attempted to clarify the issues.

This family of four had vacationed on a farm in Ireland in August 1971. Dogs, horses, and sheep were present, but cats were not mentioned. In October the mother developed cervical lymphadenopathy and

slight fever. A biopsied node was reported to be suggestive of toxoplasmosis. Her serum, obtained in November 1971, had a dye-test titer of 1:512. When this rose to 1:2,000 at the end of December she received a course of chemotherapy. The titer continued to rise. In late January the children were examined and both were found to have enlarged cervical glands. They were clinically well and "the physician thought the lymphadenopathy due to upper respiratory infections." The boy's titer on the 31st of January was 1:8,000; the girl refused to be bled. The father had no antibodies to *Toxoplasma.*

The family had a dog and a guinea pig but no cats. A sand pit in their yard presumably was used as an outdoor lavatory by a neighbor's cat. The latter was bled at the end of May and had a dye-test titer of 1:256. A sample of sand from the pit was collected in March and *Toxoplasma* was isolated from this in laboratory mice. A subsequent sample was negative.

Now there are two critical points, apart from the long interval between the mother's clinically expressed disease—incidentally, well within the acceptable incubation period for infections acquired in Ireland—and the sand-pit study. First, there is no evidence, either in the report or the subsequent correspondence, that the mother ever handled the contents of the sand pit. The girl who refused to have blood drawn was seven years old, the boy was five. Whether, or with what frequency, either or both children used the sand pit also remains unstated. Second, if we agree that the mother and her two children had acute disease, its expression in each instance was with cervical lymphadenopathy. This well may suggest a common mechanism, but we know little, if anything, about the relation between the clinical form of toxoplasmosis and the manner in which it is acquired. I suspect that this is important and, if not related to the *route* of acquisition, probably bears some relevance to the source of parasites. Closer investigation of this question might help to further our understanding of the pathogenesis of toxoplasmosis.

In any event, despite the interesting reports by Gordon Wallace and J. K. Frenkel and his colleagues on cats, soil, distribution, flies, roaches, etc., we cannot recommend more than that meat should be heated thoroughly and that cats which are allowed to eat food other than that provided in the home should not have their excreta handled by pregnant women. It should be stated also that we still lack evidence to suggest that

crawling infants and children acquire infections more readily than older children or adults, even in warm areas.

Last, I am intrigued by Dr. Frenkel's statement: "Since infection is more likely to become disease in children and the unborn, it is especially desirable to prevent the infection of children and pregnant women." I am unaware that disease (illness?) is more likely to occur in children than in adults. If this is true in any particular locality, it would lend further support to our belief that it is necessary to determine epidemiologic relations in a given area in order to formulate rational recommendations for limiting exposure in the attempt to prevent illness or congenital complications. Until we can account for many, if not all of the exceptions, such as infections in places without cats, etc., we would do well to avoid being boxed in by a single explanation for a multifaceted problem.

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